REMARKS

Claims 1-13 and 25-34 are under consideration. Solely to facilitate prosecution and without prejudice or disclaimer, Applicants have amended claims 1 and 34 to indicate that the claimed compound is glycosylated. Exemplary support for this amendment may be found in the specification at pages 6 and 7 and in the originally filed claims. Thus, this amendment does not introduce new matter. Applicants have also amended claim 30 to correct a typographical error.

Applicants acknowledge with appreciation the Office's withdrawal of all previous rejections under 35 U.S.C. § 112, first and second paragraphs; withdrawal of the rejection of claim 34 as anticipated by Bagshawe (WO 93/13805); withdrawal of the rejection of claims 1, 11, 12, 31, and 32 as obvious over Bosslet or Seemann or Eaton in view of Huston and Bosslet 2 and in further view of Ong et al. (*Can. Res.* 51:619 (1991); "Ong") and Bagshawe et al. (WO 89/10140; "Bagshawe 3"); withdrawal of the rejection of claims 1, 10, 13, and 29 as obvious over Bosslet or Seemann or Eaton in view of Huston, Bosslet 2, Bagshawe 3, Ong, and in further view of Goochee et al. (*Biotechnol.* 9:1347 (1991); "Goochee"); withdrawal of the rejection of claims 1, 2, 9, 11, 12, 31, and 32 obvious in light of Winter in view of Huston and in further view of Ong and Bagshawe 3; and the Office's withdrawal of the rejection of claims 1, 10, 13, and 29 as obvious in light of Winter in view of Huston, Ong, Bagshawe 3 and in further view of Goochee.

Claims 10-13, 29, 31, and 32 are objected to because they are dependent on rejected claims. Applicants request reconsideration of these claims in light of the arguments set forth below regarding the currently rejected claims.

The Office maintains its rejection of claim 34 as allegedly anticipated by Hellstrom et al. (U.S. Patent 5,869,045; "Hellstrom") and Borstel et al. (U.S. Patent 6,258,360; "Borstel"). The Office also maintains several rejections under 35 U.S.C. § 103, as discussed below. Applicants respond below to each of these remaining rejections according to their statutory origin.

Rejections Under 35 U.S.C. §102

The Office maintains its rejection of claim 34 under 35 U.S.C. § 102(e) as allegedly anticipated by Hellstrom. The Office believes that Hellstrom teaches a fusion polypeptide with an sFv binding portion linked to a prodrug activating enzyme by a synthetic linker. Applicants traverse.

Arguendo, even if the Office's interpretation of Hellstrom were correct, this reference does not discuss the glycosylation of such protein constructs. Claim 34, as amended, clearly indicates that the resulting claimed compound is glycosylated. Because Hellstrom does not teach this claim element, claim 34 is not anticipated by this reference. Applicants request that this rejection be withdrawn.

Claim 34 stands rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Borstel. According to the Office, Borstel describes fusion proteins that contain a single chain antibody and an enzyme that activates a prodrug. The Office further notes that Borstel's constructs contain a polypeptide linker sequence. Applicants contend that Borstel does not anticipate claim 34.

Borstel does not teach glycosylation of the "immunoconjugates" discussed therein. See col. 7, lines 4-9. Rather, the core of Borstel's invention is to develop prodrugs that can be activated by catalytic proteins. Where Borstel teaches glycosyl

groups or glycosylation, it is in reference to the prodrugs themselves, not to the immunoconjugate. See, e.g., col. 14, lines 34 and 35; col. 40, lines 9, 34-35, 41, and 45-46; and col. 49, lines 35 and 36. As claim 34 recites a compound comprising two or more antigen binding regions linked to at least one prodrug-activating enzyme wherein the compound is glycosylated and Borstel does not teach glycosylation of such a compound, this reference cannot anticipate claim 34. Applicants request that the Office withdraw its rejection of this claim.

Rejections Under 35 U.S.C. §103

The Office maintains its rejection of claims 1-9, 25-28, 30, 33, and 34 under § 103(a) in two general groups: one in which Bosslet et al. (*Brit. J. Can.* 65:235 (1992); "Bosslet"); Seemann et al. (Canadian Patent 2,062,047; "Seemann"); and Eaton et al. (EP 392,745; "Eaton") are the primary references and a second in which Winter is the primary reference. Applicants address these rejections according to their groups below with respect to independent claims 1 and 34.

Rejections based on Bosslet, Seemann, Eaton, Huston, and Bosslet 2

The remaining rejections in this group are as follows:

1. Claims 1-9, 25-27, 30, 33, and 34 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Bosslet or Seemann or Eaton in view of Huston et al. (U.S. Pat. 5,258,498; "Huston") and Bosslet et al. (U.S. Pat. 5,591,828; "Bosslet 2"). According to the Office, Bosslet and Seemann both teach a fusion protein comprising a Fab, a linker, and a human β-glucuronidase. The Office also alleges that Eaton teaches a fusion protein comprising a Fab and an *E. coli* β-lactamase.

2. Claims 1 and 28 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Bosslet or Seemann in view of Huston, Bosslet 2, Eaton, and in further view of Bagshawe et al. (WO 88/07378; "Bagshawe 2"). The Office believes that Bagshawe 2 provides that it was known and conventional to provide carboxypeptidase G2 from *Pseudomonas* as a prodrug activating enzyme.

Applicants respectfully traverse the above two rejections. Claim 1 and claim 34 both recite that the claimed compound is glycosylated. Applicants previously successfully argued that the references listed in the two rejections above in combination with three additional references, Ong , Bagshawe 3, and Goochee, did not make glycosylation or mannosylation of the claimed compounds obvious. In the current Office Action, the Office withdraws its rejections based on these references, noting that

> Examiner concurs that Huston et al. does not discuss the impact of glycosylation upon the sFv constructs. Due to their much smaller size, as compared to antibodies, it is not predictable as to whether or not these would retain binding activity upon glycosylation.

Current Office Action at page 5. Because the Office has agreed with Applicants that Bosslet or Seemann in view of Huston, Bosslet 2, Eaton, and Bagshawe 2 (even when combined with Ong, Bagshawe 3, and Goochee) cannot make glycosylation obvious, claims 1 and 34, which recite glycosylation, cannot be rendered obvious by these references or a subset of these references. Applicants respectfully request that the Office withdraw its rejection of claims 1-9, 25-28, 30, 33, and 34.

Rejections based on Winter

The Office maintains its rejections of the pending claims 1-9, 25-28, 30, 33, and 34 under 35 U.S.C. §103(a) in view of Winter et al. (U.S. Patent 6,248,516; "Winter") and a combination of other references. These rejections are as follows:

1. Claims 1-4, 8, 9, 25, 26, 32, 33, and 34 are rejected as allegedly obvious in light of Winter in view of Huston. According to the Office, Winter teaches single domain ligands, including sFv fragments, that can be linked to an effector molecule such as a prodrug activating enzyme. Winter also allegedly teaches that the single domain ligands may be present in multiple copies. The Office acknowledges, however, that Winter does not clearly teach whether there is a linker between the variable domains in the sFv fragment. The Office relies on Huston to teach such a linker and more specifically, a linker with the sequence (GlyGlyGlyGlySer)3. Applicants note that the Office has applied these two references in the same manner for the additional rejections below, based on Winter.
2. Claims 1, 2, 4, 5, 7, and 9 remain rejected as allegedly obvious in light of Winter and in view of Huston and in further view of Seemann. The Office believes that Seemann teaches therapeutic fusion proteins with binding specificity to CEA and β-glucuronidase activity. The Office then asserts that CEA is a known tumor antigen and β-glucuronidase is a known pro-

drug activating enzyme and concludes that it would have been obvious to combine these activities with Winter's single domain ligand constructs.

3. Claims 1, 6, 27, and 30 remain rejected as allegedly obvious in light of Winter in view of Huston and in further view of Eaton. Specifically, the Office contends that while Winter does not teach β-lactamase as a pro-drug activating enzyme, Eaton teaches that such enzymes were known in the art in the context of antibody conjugates. Thus, according to the Office, it would have been obvious to use this enzyme in the context of Winter's sFv compositions.
4. Claims 1, 6, and 28 remain rejected as allegedly obvious in light of Winter in view of in view of Huston and in further view of Bagshawe 2. According to the Office, Winter does not teach carboxypeptidase G2 as a prodrug activating enzyme but Bagshawe 2 demonstrates that this enzyme was a known prodrug activating enzyme. Thus, the Office believes that it would be obvious to use this enzyme in the context of Winter's single domain ligand constructs.

Applicants refer to their discussion above with respect to the first group of rejections based on obviousness. The addition of Winter to the list of references recited in the first group does not make the glycosylation of the compounds of claims 1 and 34 obvious. The Office apparently agrees with Applicants' position, as demonstrated by its withdrawal of obviousness rejections based on Winter, Huston, Ong, Bagshawe 3 and Goochee. See current Office Action at page 7. Applicants therefore request that the rejection of claims 1-9, 25-28, 30, 33, and 34 be withdrawn.

Conclusion

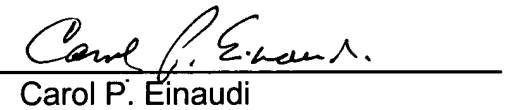
In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of claims 1-13 and 25-34.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: May 3, 2004

By: 

Carol P. Einaudi
Reg. No. 32,220